UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,669	04/09/2004	M. Zouhair Atassi	17525 (AP)	9880

51957 7590 12/20/2005

ALLERGAN, INC., LEGAL DEPARTMENT
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/821,669	ATASSI, M. ZOUHAIR	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/9/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-133* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-133* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-133 are pending.

Information Disclosure Statement

1. The information disclosure statement filed October 1, 2004 and April 25, 2005 have been considered.

Claim Objections

1. Claims 1-47 are objected to for minor informalities:

2. Claims 1-47 recite terms set forth in brackets and it is not clear whether these terms are intended to be positively recited claims limitations. Are they are abbreviations or possible claim limitations?

3. Claims 1-47 recite Markush groups, the species of which are set apart by semi-colons; they should be set apart by commas A, B, C and D. Additionally the Markush groups are not recited in the format A, B, C and D, but is improperly recited A; B;C; D; E; or F or G.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31-43, 84-92,114-122 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods and compositions for the induction of an immune response, does not reasonably provide enablement for induction of a protective immune response through administering a peptide that is an immunoreactive fragment or conservative variant, or a peptide that does not induce a protective immune response there to. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. The instant Specification describes numerous peptide epitopes contained in botulinum toxin heavy chain, both the N-terminal and C-terminal domains. The Specification also teaches the production of monoclonal and polyclonal antibodies to specific peptides, but does not provide evidence that any of these peptides alone can serve to induce a protective immune response in vivo, especially when the peptide is not conjugated to an immunogenic carrier, and is not sufficiently large to be recognized as foreign in an immunocompetant host animal. Immunoreactive fragments of a peptide could be as small as 1-3 amino acids, and would be far too small to induce an immune response by itself, no less a protective immune response which is a required functional characteristic of a vaccine.

7. The specification fails to teach how to formulate and use the claimed vaccines. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction. Dertzbaugh et al (1996) evaluated various botulinum toxin peptide fragments, and only found two fragments to induce protection against challenge with botulinum toxin. The Dertzbaugh et al fragments were larger than 60 amino acids and were successful in providing definitive protection (see page 1541, col. 2, Dertzbaugh et al, 1996).

The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing infections and/or neurotoxicity due to a neurotoxin producing pathogen. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed

vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. While the peptides of Dertzbaugh all induced an immune response, only two were found to provide protection. Additionally, Oshima et al (1997) administered peptides from the heavy chain of botulinum toxin and extensive variance in immune response based upon the animal to which the peptides were administered. Balb-C mice were found not to recognize several of the peptide that were found to be immunogenic in SJL mice; variability in immune response introduces an element of unpredictability for a peptide compositions, especially when it must induce a protective immune response (see Oshima et al, Tables 2 and 3, pages 10-11).

The ability to reasonably predict the capacity of a single bacterial peptide to induce protective immunity from in vitro antibody reactivity studies is problematic. Ellis exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of a protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al. wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response is s induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

The specification fails to teach the identity of conservative variants, and what immunoreactive fragments of the peptides and conservative variants would serve to function as a protective peptide upon administration to a host animal. Further, the specification fails to provide an adequate written description of other amino acids sequences that would induce a protective immune response, the skilled artisan would be required to de novo locate, identify and

characterize the claimed other peptides. This would require undue experimentation given the fact that the specification is completely lacking in teachings as to other surface proteins with the claimed characteristics.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-47, 54-133 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-47 recite the phrase "conservative variant". How the antibody binding would be indicative of botulinum toxin therapy when is binds to a variant sequence that need not be specific to botulinum toxin therapy is specifically or distinctly claimed. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. See In re Mayhew.

10. Claims 54-133 are directed to methods and compositions that comprise a BoNT/A peptide have a length of 60 amino acids, but all of the ranges of amino acids recited in the claims are about 26-27 amino acids in length; what are the additional 23-24 amino acids not recited in the claims? The invention is not distinctly claimed in light of all of the recited ranges of amino acids of SEQ ID NO 1, being less than 60 amino acids and the claimed peptides may be up to 60 amino acids in length. What amino acids are the antibodies immunoreactive with if not with the

recited range of amino acids? The antibodies may bind the additional amino acids, "antibodies immunoreactive with a BoNT/A peptide having a length of at most 60 amino acids", but what the additional amino acids are that are not recited in the claims, is not positively, nor clearly and distinctly claimed. The meets and bounds of the claim are not clearly defined by the combination of claim limitations set forth therein. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 1-4, 14,16-17,31-34,54,56-60,63-70,72,73,84-91,93-99,114-120,123,125-129,132 is rejected under 35 U.S.C. 102(b) as being anticipated by Rosenberg et al (1996).

Rosenberg et al disclose the instantly claimed invention directed to a method that comprises the steps of :

Determining the presence or absence of antibodies immunoreactive with a peptide (see

peptide 1, Figure 1, page 493) or two or more amino acid sequences (see page 497, Table 1), wherein the antibodies reacted with the peptides in an immunoassay (RIA, page 494, paragraph 4), and therefore immunoreacted with an immunoreactive fragment of the disclose peptides (reads on a single amino acid held in common). The immunoassays used to determine the presence or absence of the antibodies immunoreactive with two or more of the amino acid sequences included rabbit antimouse IgG antibodies (see page 494, paragraph 4).

Vaccine compositions comprising an adjuvant were formulated (see page 494, paragraph 2"). The presence of antibodies was determined through removing blood, and contacting the antibody containing blood component (serum) with two or more amino acid sequences that comprise the recited range of amino acids (see Tables 1 and Figure 4).

The peptide/proteins were immobilized on a solid surface and when the antibodies bound thereto, they were removed from the blood-containing component upon formulation of an antibody/amino acid sequence complex (see page 494, paragraph 4 "solid-phase radioimmunoassay" and "extensively washed with PBS"). The reference anticipates the instantly clamed invention.

3. Claims 1, 5-13, 15,17,31-47, 54-62,64-65,84-101, 114-132 are rejected under 35 U.S.C. 102(b) as being anticipated by Dertzbaugh et al (1996).

Dertzbaugh et al disclose the instantly claimed invention directed to a method that comprises the steps of :

Determining the presence or absence of antibodies immunoreactive with two or more amino acid sequences (see page 1540, Figure 1), wherein the antibodies reacted with the peptides

in an immunoassay (immunoblot, see Figure 2; Tables 1-2 page 1541, column 1, last half of paragraph 2 "H630-808 each appeared to elicit antibody that recognized a determinant located in all of the other serotypes of BoNT tested"). The immunoassays used to determine the presence or absence of the antibodies immunoreactive with two or more of the amino acid sequences included ELISA and immunoblot (see page 1541, column 1, header). Vaccine compositions comprising an adjuvant were formulated (see page 1539, col. 2, paragraph 2; page 1540, column 2 "All of the truncated proteins were able to elicit and antibody response to the appropriate chain "). The presence of antibodies was determined through removing blood, and contacting the antibody containing blood component (serum) with two or more amino acid sequences that comprise the recited range of amino acids (see Tables 1 and 2 and immunoblot. The peptide/proteins were immobilized on a solid surface and when the antibodies bound thereto, they were removed from the blood-containing component upon formulation of an antibody/amino acid sequence complex.

The reference anticipates the instantly clamed invention.

4. Claims 18-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Allison (US 2002/0197278 A1, December 26, 2002).

Allison described the instantly claimed invention directed to a method that comprises the step of :

administering a tolerogizing agent, specifically polyethylene glycol together with two or more amino acid sequences of SEQ ID NO 1, wherein the amino acid sequences are linked together into botulinum toxin A polypeptide (see title, abstract, paragraph [0007] "The reduced

immunogenicity of pegylated toxin will decrease the development of resistance"). The reference anticipates the instantly claimed invention as now claimed.

5. Claims 31-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Oshima et al (1998).

Oshima et al disclose the instantly claimed method, the method comprising the step of:

vaccinating an individual with two or more amino acid sequences (see Table 1, page 8 "peptide mixtures) combined with an adjuvant (see section 2.2), wherein an immune response was produced (see section 2.4, page 8 and Tables 2-3). The reference anticipates the instantly claimed invention

6. Claims 44 is rejected under 35 U.S.C. 102(b) as being anticipated by Oshima et al (1997).

Oshima et al (1997). Oshima et al disclose the instantly claimed invention directed to a method that comprises the steps of:

removing blood from a patient ("sera were collected" page 1032, column 2, paragraph 1); contacting the antibody-containing component of the blood with immunoreactive peptides (see Table 1, peptides 1-31) to form a complex;

removing the complex from the antibody-containing component thereof ("washed", page 1032, column 2, middle of last paragraph; also see competitive inhibition with soluble peptides page 1035, Figure 2, Figure 4, Figure 5, page 1038, column 2, paragraph 1).

The reference anticipates the instantly claimed invention.

7. Claims 44-47 is rejected under 35 U.S.C. 102(b) as being anticipated by Singh et al (1996).

VS/
1/10/05

8. Singh et al disclose the instantly claimed invention directed to a method that comprises the steps of:

removing blood from a patient (see page 269, Materials, first paragraph "serum");

contacting the antibody-containing component of the blood with an amino acid sequence comprising a sequence of two or more peptides (see page 269 "Type A" paragraph 1; and paragraph 3 "affinity purified") to form a complex;

removing the complex from the antibody-containing component thereof(affinity purified complex, page 269, paragraph).

The reference inherently anticipates the instantly claimed invention.

9. Claims 48-50 and 52-53 is rejected under 35 U.S.C. 102(b) as being anticipated by Naumann et al (1998).

10. Naumann et al disclose the instantly claimed invention directed to a method that comprises the step of:

determining the level of IgG antibodies immunoreactive with botulinum toxin and comparing the level with a control level of IgG antibodies (page 924, column 2, last paragraph, page 925, Figure 1 and all narrative on page "Total IgG" measured before and after IA-PA; "virtually all neutralizing antibodies were contained in the IgG class; page 926, Figure 2, all narrative on page). The titer values for IgG were reduced and then increased over 10 fold (see Figure 2). The reference anticipates the instantly claimed invention.

11. Claims 48 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Oshima et al (1998).

Oshima et al disclose the instantly claimed invention directed to a method that comprises the steps of:

a. Determining the level of IgG antibodies immunoreactive with botulinum toxin in said individual (see page 8, col. 2, section 2.4 "IgG" antibodies determined; and

b. Comparing the level of IgG antibodies to a control level of IgG antibodies, wherein the control level of antibodies is determined in an individual who has not been treated with botulinum toxin therapy (see page 8, col. 1, section 2.2 "sera were collected prior to the first injection. The reference anticipates the instantly claimed invention as now claimed.

12. Claims 84, 86-87, 88-94, 95-100, 114, 116-121,123,125-130,132 are rejected under 35 U.S.C. 102(b) as being anticipated by Bavari et al (1998)

Bavari et al disclose the instantly claimed invention directed to peptide compositions that comprise an adjuvant, and methods that comprise the step of administering a peptide composition that comprises amino acids from the range of 445-471 of SEQ ID NO 1, and has a length of at most 60 amino acids.

The peptide composition of Bavari et al was amino acids 449-473 of the N-terminal of botulinum toxin A heavy chain (see sequence in Table 3, page 1853), The composition was formulated with KLH or other adjuvants (see page 1854, col. 2, paragraph 2, last two sentences of paragraph). The administered peptide induced an immune response (see Figure 4, frame D, titer dilution to 10^4. The antibodies were polyclonal antibodies. The composition and method of Bavari et al anticipates the instantly claimed invention as now claimed.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 74-83 and 102-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allison (US 2002/0197278 A1, December 26, 2002) in view of Oshima et al.

See discussion of Allison above. Allison describe and show compositions that comprise a tolerogizing agent, specifically polyethylene glycol together with two or more amino acid

sequences of SEQ Id NO 1, and methods of administering the composition to an individual, but differs from the instantly claimed invention by failing to show the amino acid sequences to be in the form of a mixture of peptides.

Oshima et al teach compositions that comprise two or more amino acid sequence of SEQ ID NO 1 formulated together into compositions are a mixtures of peptides in an analogous art for the purpose of producing and determining an immune response directed to botulinum toxin A.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the compositions and method of Allison with the peptides of Oshima et al because both Allison and Oshima are directed to the production of compositions that comprise amino acid sequences of botulinum toxin A, and Oshima et al teach the administration of specific immunogenic peptides that comprise the epitopes present in botulinum toxin A and Oshima et al teach that the peptides provide the advantage of induced a possible cross-protective immune response against more than one botulinum neurotoxin (see abstract last few lines), and Allison teaches the advantage of combining a tolerogizing agent with the botulinum toxin amino acid sequence because the tolerogizing agent increases the molecular weight of the immunogen administered, decreases the diffusion of the composition from the site of administration, reduces the immunogenicity of the antigen and decreases the likelihood of developing resistance to the botulinum toxin (see Allison, page 1, [0007] last few lines). Allison in view of Oshima et al obviates the instantly claimed invention.

15. Claims 102 and 112-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allison (US 2002/0197278 A1, December 26, 2002), in view of Atassi et al (US Pat. 6,048,529).

See discussion of Allison above. Allison describe and show compositions that comprise a

tolerogizing agent, specifically polyethylene glycol (PEG) together with two or more amino acid sequences of SEQ Id NO 1, and methods of administering the composition to an individual, but differs from the instantly claimed invention by failing to show the tolerogizing agent to be mPEG or polyvinyl alcohol.

Atassi et al teach compositions that comprise a tolerogizing agent, wherein the tolerogizing agent is mPEG or polyvinyl alcohol in an analogous art for the purpose of preventing undesirable immune responses to an administered epitope peptide.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the compositions and method of Allison with tolerogizing agent of Atassi et al because both Allison and Atassi et al are directed to the production of compositions that comprise amino acid sequences of botulinum toxin A, together with a tolerogizing agent and Atassi et al teaches additional tolerogizing agents that have been shown to successfully prevent the induction of an undesired immune response to an epitope or peptide. In the absence of a showing of unexpected results, Allison in view of Atassi et al obviates the instantly claimed invention.

16. Claim 71 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenberg et al in view of Dertzbaugh et al.

See discussion of Rosenberg et al above. Rosenberg et al describe a method of determining the presence or absence of antibodies immunoreactive to botulinum neurotoxin A peptides utilizing an immunoassay, but differs from the instantly claimed invention by failing to show the immunoassay to be an ELISA.

Dertzbaugh et al describe an ELISA for determining the presence or absence of antibodies immunoreactive to botulinum neurotoxin A in an analogous art for the purpose of detecting the antibodies to botulinum neurotoxin A peptides (see Table 1 and col. 1, page 1541).

It would have been obvious to the person of ordinary skill in the art the time the invention was made, to modify the immunoassay method of Rosenberg et al to include the ELISA immunoassay method of Dertzbaugh et al because the ELISA method of Dertzbaugh et al is a non-radioactive method of detecting the presence of antibodies in a sample containing antibodies and therefore does not require special handling of radioactive waste, and the ELISA successfully detected the presence of antibodies directed to botulinum neurotoxin A peptides associated with a protective immune response (see Table 1). Rosenberg et al in view of Dertzbaugh et al obviates the instantly claimed invention.

17. Claims 123 and 133 are rejected under 35 U.S.C. 103(a) as being obvious over Kubota et al (1997) in view of Harlow (1988, reference cited in Applicant's specification).

Kubota et al teach monoclonal antibodies that were collected and processed and shown to immunoreact with an epitope in Hn domain of Clostridium botulinum toxin, and comprises a conservative variant of the amino acids in the range of 655-681 of SEQ ID NO 1 (see Kubota et al, Table 5, imunoreactivity of LE34-6 over 6 amino acids in the range from 640-690)

While it is well known in the art that monoclonal antibodies are produced by the method steps of administering to an animal a BoNT/A conservative variant of the amino acid range 655-681, wherein the epitope was found to be within this range in BoNT/E (see Table 5, page 1217),

Collecting from the animal a sample containing an antibody or antibody producing cell,

and

Processing the sample to isolate the antibody, Kubota et al is silent with respect to the specific steps used to obtain the monoclonal antibodies.

Harlow teaches means and methods of producing monoclonal antibodies to peptide in an analogous art for the purpose of obtaining a ready, well-defined source of highly specific antibodies for diagnostic and medical purposes.

It would have been obvious to the person of at the time the invention was made to obtain monoclonal antibodies at taught by Kubota et al to the epitope within the range of amino acids from 655-681 as described and shown to be immunogenic, in view of the guidance and teachings of Harlow et al because the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining additional monoclonal antibodies with binding specificities for Clostridium botulinum toxin a conservative variant amino acid sequence of 655-681 of SEQ ID NO 1 in view of the fact that Kubota et al successfully collected and processed a sample to obtain monoclonal antibodies with binding specificity to an epitope of the botulinum toxin that also evidenced neutralizing activity.

In the absence of a showing of unexpected results, Kubota et al in view of Harlow obviate the instantly claimed invention as now claimed. See In re Erlich 1988.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
November 21, 20905

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600